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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/645,723	08/21/2003	Charles Mark Ensor	PHOE-0136	8074

23377 7590 03/24/2006

WOODCOCK WASHBURN LLP
ONE LIBERTY PLACE, 46TH FLOOR
1650 MARKET STREET
PHILADELPHIA, PA 19103

EXAMINER	
RAMIREZ, DELIA M	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 03/24/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/645,723	ENSOR ET AL.	
	Examiner	Art Unit	
	Delia M. Ramirez	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *71-75* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *71-75* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *21 August 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *10/27/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *alignment*.

DETAILED ACTION

Status of the Application

Claims 71-75 are pending.

Applicant's preliminary amendment canceling claims 1-71, and amendments to the specification which bring the application in compliance with sequence rules, as submitted in a communication filed on 8/21/2003 are acknowledged.

Specification

1. The specification is objected to for the following reasons. While the first paragraph of the specification provides a list of related cases, the status of U.S. Application No. 09/564559 has not been updated (now U.S. Patent No. 6635462). Appropriate correction is required.

2. The specification is objected to for the following reasons. The location shown for the American Type Culture Collection on page 13, line 17, and on page 16, line 7 is incorrect. Appropriate correction is required.

3. The specification is objected to due to the recitation of "rom" in line 6, page 16 and "pudita" in page 2, lines 5 and 17. They appear to be a typographical errors. Appropriate correction is required.

4. The specification is objected to due to the recitation of "hominus" (at least 30 occurrences) throughout the specification. The term should be replaced with "hominis". Appropriate correction is required.

5. The use of trademarks has been noted in this application. See, for example "Altered sites II" on page 16, line 10. They should be capitalized wherever it appears and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Priority

6. Acknowledgment is made of a claim for domestic priority under 35 U.S.C. 119(e) to provisional application No. 60/046,200 filed on 05/12/1997.

7. Acknowledgment is made of a claim for domestic priority under 35 U.S.C. 120 or 121 to US application No. 09/564,559 filed on 05/04/2000, and 09/023,809 filed on 02/13/1998.

8. It is noted that an *M. hominis* arginine deiminase modified by elimination of at least one pegylation site at or adjacent to the catalytic region of the deiminase has been first disclosed in U.S. Application No. 09/564,559, filed on 05/04/2000.

Information Disclosure Statement

9. The information disclosure statement (IDS) submitted on 10/27/2003 is acknowledged. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the Examiner.

Drawings

10. The drawings submitted on 8/21/2003 have been reviewed and are accepted by the Examiner.

Claim Objections

11. Claims 71-75 are objected to due to the recitation in claim 71 of "arginine deiminase....catalytic region of the polypeptide". While it is understood that the "polypeptide" recited refers to the arginine deiminase claimed, for clarity and consistency within the claim, it is suggested that the term "polypeptide" be replaced with "arginine deiminase" or "deiminase". Appropriate correction is required.

Claim Rejections - 35 USC § 112, Second Paragraph

12. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

13. Claims 71-75 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

14. Claim 71 (claims 72-75 dependent thereon) is indefinite in the recitation of "an arginine deiminase comprising arginine deiminase isolated from *Mycoplasma hominis* that has been modified..." for the following reasons. As written, it is unclear if the claimed deiminase is a deiminase which is isolated from *M. hominis* or if the claimed deiminase is a fusion protein which comprises any *M. hominis* deiminase and other unknown structural elements which would still allow the fusion protein to have that activity. For examination purposes, it will be assumed that the claim reads "an arginine deiminase isolated from *Mycoplasma hominis* that has been modified by elimination of at least one pegylation site at or adjacent to the catalytic region of the arginine deiminase". Correction/clarification is required.

15. Claim 72 (claim 75 dependent thereon) is indefinite in the recitation of "the arginine deiminase of claim 71 wherein the arginine deiminase has been modified by deletion or substitution of at least one amino acid" for the following reasons. As written, there is no indication that the deletion/substitution of at least one amino acid is related to the modification recited in claim 72 regarding the pegylation site. Therefore, it is unclear if, for example, the intended arginine deiminase is (1) the deiminase of claim 71 wherein the elimination of at least one pegylation site is obtained by deletion or substitution of at least one amino acid, or (2) the arginine deiminase of claim 71 which has been modified by (a) elimination of at least one pegylation site at or adjacent to the catalytic region of the deiminase, and (b) deletion/substitution of any number of amino acids anywhere in that deiminase (not necessarily affecting any pegylation site). For examination purposes, it will be assumed that claim 72 is directed to an arginine deiminase from any source which has any amino acid sequence wherein said arginine deiminase has less

pegylation sites at or adjacent to the catalytic region than a *M. hominus* arginine deiminase. It is noted that the limitation regarding the source of the deiminase in claim 71 (*M. hominis*) is not given patentable weight in view of the fact that any number of deletions/substitutions will result in a protein having any amino acid sequence which no longer resembles that originally isolated from *M. hominis* and can potentially be a protein that can be found in another organism. Correction is required.

Claim Rejections - 35 USC § 112, First Paragraph

16. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

17. Claims 71-75 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 71, 73-74, and 75 (in part) are directed to a genus of *M. hominis* arginine deiminases that have been modified by elimination of at least one pegylation site at or adjacent to the catalytic region of the deiminase. Claims 72 and 75 (in part) are directed to any arginine deiminase wherein said deiminase does not have pegylation sites at or adjacent to the catalytic region of the deiminase. See Claim Rejections under 35 USC 112, second paragraph, for claim interpretation.

In *University of California v. Eli Lilly & Co.*, 43 USPQ2d 1938, the Court of Appeals for the Federal Circuit has held that "A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials". As indicated in MPEP § 2163, the written description requirement for a claimed genus may be satisfied

through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show that Applicant was in possession of the claimed genus. In addition, MPEP § 2163 states that a representative number of species means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus.

There is no actual structural limitation with regard to the members of the genus of proteins claimed. While the specification in the instant application discloses the structure of a single species of the claimed genus of *M. hominis* arginine deiminases, i.e. the polypeptide of SEQ ID NO: 1, and there are some arginine deiminases from other sources known in the art, neither the specification nor the art provide a clue as to the structural elements required in any arginine deiminase or any *M. hominis* arginine deiminase, nor do they teach which structural elements of the polypeptide of SEQ ID NO: 1 are required in any arginine deiminase (or *M. hominis* arginine deiminase) as claimed. The specification fails to describe any additional species by any relevant, identifying characteristics or properties other than by functionality (i.e., arginine deiminase activity).

The claim encompasses a genus of proteins which is structurally unrelated. A sufficient written description of a genus of polypeptides may be achieved by a recitation of a representative number of polypeptides defined by their amino acid sequence or a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus. However, in the instant case, there is no structural feature which is representative of all the members of the genus of proteins recited in the claim, and there is no information as to a correlation between structure and function. Furthermore, while one could argue that SEQ ID NO: 1 is representative of the structure of all

the members of the genus, such that the recited genus of polypeptides is adequately described by the disclosure of the structure of the polypeptide of SEQ ID NO: 1, it is noted that the art teaches (1) several examples of how even small changes in structure can lead to changes in enzymatic function, and (2) structural variation among arginine deiminases from the same organism. For example, Witkowski et al. (Biochemistry 38:11643-11650, 1999) teaches that one conservative amino acid substitution transforms a β-ketoacyl synthase into a malonyl decarboxylase and completely eliminates β-ketoacyl synthase activity. Seffernick et al. (J. Bacteriol. 183(8):2405-2410, 2001; cited in the IDS) teaches that two naturally occurring Pseudomonas enzymes having 98% amino acid sequence identity catalyze two different reactions: deamination and dehalogenation, therefore having different function. Filpula et al. (WO 98/33519; published 8/6/1998; cited in the IDS) teach that there are several arginine deiminases in *Mycoplasma arthritidis* and that there are dramatic differences among these arginine deiminases in a number of fundamental properties. Filpula et al. suggest that the different arginine deiminases found in *Mycoplasma arthritidis* are the products of more than one gene (page 3, line 21-page 4, line 13). Therefore, since minor structural changes to a polypeptide may result in changes affecting function, no additional information correlating structure with arginine deiminase activity has been provided, and no structure has been provided which is representative of all *M. hominis* arginine deiminases, one cannot reasonably conclude that SEQ ID NO: 1 is representative of the structure of all arginine deiminases as recited in the claims.

Due to the fact that the specification only discloses a single species of the genus of *M. hominis* arginine deiminases, i.e. the polypeptide of SEQ ID NO: 1, and the lack of description of any additional species by any relevant, identifying characteristics or properties, one of skill in the art would not recognize from the disclosure that Applicant was in possession of the claimed invention.

18. Claims 71-75 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the arginine deiminase of SEQ ID NO: 1 wherein said arginine deiminase has been modified, wherein said modification consists of eliminating at least one pegylation site at or adjacent to the catalytic region, does not reasonably provide enablement for (1) any arginine deiminase isolated from *Mycoplasma hominis* that has been modified by elimination of at least one pegylation site at or adjacent to the catalytic region of the deiminase, or (2) any arginine deiminase wherein said deiminase does not have pegylation sites at or adjacent to the catalytic region of the deiminase. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required are summarized in *In re Wands* (858 F.2d 731, 737, 8 USPQ2nd 1400 (Fed. Cir. 1988)) as follows: 1) quantity of experimentation necessary, 2) the amount of direction or guidance presented, 3) the presence and absence of working examples, 4) the nature of the invention, 5) the state of prior art, 6) the relative skill of those in the art, 7) the predictability or unpredictability of the art, and 8) the breath of the claims. The factors which have lead the Examiner to conclude that the specification fails to teach how to make and/or use the claimed invention without undue experimentation, are addressed in detail below.

The breath of the claims. Claims 71-75 are so broad as to encompass (1) any arginine deiminase isolated from *Mycoplasma hominis* that has been modified by elimination of at least one pegylation site at or adjacent to the catalytic region of the deiminase, or (2) any arginine deiminase wherein said deiminase does not have pegylation sites at or adjacent to the catalytic region of the deiminase. See Claim Rejections under 35 USC 112, second paragraph, for claim interpretation. The enablement provided is not commensurate in scope with the claims due to the extremely large number of proteins of unknown structure encompassed by the claim. In the instant case, the specification enables a single species, i.e., the polypeptide of SEQ ID NO: 1.

The amount of direction or guidance presented and the existence of working examples. The specification discloses the amino acid sequence of a single protein (SEQ ID NO: 1) and specific changes to the polypeptide of SEQ ID NO: 1 which would result in elimination of pegylation sites, as a working example. However, the specification fails to provide any clue as to the structural elements required in any arginine deiminase or any *M. hominis* arginine deiminase, or which are the structural elements in the polypeptide of SEQ ID NO: 1 that are essential for any protein to display arginine deiminase activity. No correlation between structure and arginine deiminase activity has been presented.

The state of prior art, the relative skill of those in the art, and the predictability or unpredictability of the art. The amino acid sequence of a polypeptide determines its structural and functional properties. While the art discloses several proteins having arginine deiminase activity, neither the specification nor the art provide a correlation between structure and arginine deiminase activity such that one of skill in the art can envision the structure of any arginine deiminase or any *M. hominis* arginine deiminase. In addition, the art does not provide any teaching or guidance as to (1) which changes can be made to the protein of SEQ ID NO: 1 such that the resulting variant would display arginine deiminase activity, or (2) the general tolerance of arginine deiminases to structural modifications and the extent of such tolerance. The art clearly teaches that modification of a protein's amino acid sequence to obtain the desired activity without any guidance/knowledge as to which amino acids in a protein are tolerant of modification and which ones are conserved is highly unpredictable. At the time of the invention there was a high level of unpredictability associated with altering a polypeptide sequence with an expectation that the polypeptide will maintain the desired activity. For example, Branden et al. (Introduction to Protein Structure, Garland Publishing Inc., New York, page 247) teach that (1) protein engineers are frequently surprised by the range of effects caused by single mutations that they hoped would change only one specific and simple property in enzymes, (2) the often surprising results obtained by experiments where single mutations are made reveal how little is known about the rules of protein stability, and (3) the

difficulties in designing *de novo* stable proteins with specific functions. The teachings of Branden et al. are further supported by the teachings of Witkowski et al. (Biochemistry 38:11643-11650, 1999), Seffernick et al. (J. Bacteriol. 183(8):2405-2410, 2001) and Filpula et al. already discussed above, where it is shown that even small amino acid changes result in enzymatic activity changes and the unexpected variability found among arginine deiminases of the same organism.

The quantity of experimentation required to practice the claimed invention based on the teachings of the specification. While methods of generating or isolating variants of a polypeptide were known in the art at the time of the invention, it was not routine in the art to screen by a trial and error process for all polypeptides having arginine deiminase activity. In the absence of (1) a rational and predictable scheme for modifying any residue in the polypeptide of SEQ ID NO: 1 such that the resulting variant would maintain arginine deiminase activity, and/or (2) a correlation between structure and arginine deiminase activity, one of skill in the art would have to test an essentially infinite number of proteins to determine which ones have arginine deiminase activity.

Therefore, taking into consideration the extremely broad scope of the claim, the lack of guidance, the amount of information provided, the lack of knowledge about a correlation between structure and the desired function, and the high degree of unpredictability of the prior art in regard to structural changes and their effect on function, one of ordinary skill in the art would have to go through the burden of undue experimentation in order to practice the claimed invention. Thus, Applicant has not provided sufficient guidance to enable one of ordinary skill in the art to make and use the invention in a manner reasonably correlated with the scope of the claims.

Claim Rejections - 35 USC § 102

19. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

20. Claims 72 and 75 are rejected under 35 U.S.C. 102(b) as being anticipated by Filpula et al. (WO 98/33519; published 8/6/1998; cited in the IDS). As indicated above in Claim Rejections under 35 USC 112, second paragraph, claim 72, as interpreted, is directed to any arginine deiminase from any source having any amino acid sequence (by virtue of allowing any number of deletions/substitutions) wherein said deiminase has less pegylation sites at or adjacent to the catalytic region than a *M. hominus* arginine deiminase. Claim 75 is directed to a composition comprising the deiminase of claim 72 and at least one carrier, diluent, or excipient. Filpula et al. teach an arginine deiminase from *M. arthritidis* of 410 amino acids which has a region lacking lysine residues (pegylation sites) between positions 94-114 (Figure 3, line a, an arginine and alanine residue at positions 111-112 of that deiminase, respectively). The specification of the instant application on page 7, lines 24-26, teaches that (1) the *M. hominis* arginine deiminase of SEQ ID NO: 1 has a lysine residue at position 112 which is either at or adjacent to the catalytic region of the enzyme, and (2) the *M. hominis* arginine deiminase of SEQ ID NO: 1 has two lysine residues between residues 94-114 of SEQ ID NO: 1. The *M. arthritidis* (410 amino acids) arginine deiminase of Filpula et al. is only one amino acid larger that the *M. hominis* arginine deiminase of the instant application (SEQ ID NO: 1, 409 amino acids), and is 81% sequence identical to the polypeptide of SEQ ID NO: 1. See attached alignment. Therefore, absent evidence to the contrary, one would expect the amino acid at position 112 of the *M. arthritidis* arginine deiminase to be at or adjacent to the catalytic region, and amino acids 94-114 to be either adjacent to the catalytic region or overlapping the catalytic region. Filpula et al. also teach compositions comprising the deiminase and a diluent (purified recombinant ADI in refolding buffer, Example 2, page 25, lines 28-29; pegylated arginine deiminase and complete media, Example 7, page 28, lines 3-4). Therefore, the teachings of Filpula et al. anticipate claims 72 and 75 as interpreted.

Double Patenting

21. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., In re Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); In re Van Ornum, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In re Thorington, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement. Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

22. Claims 1-5 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-13 of U.S. Patent No. 6635462. Although the conflicting claims are not identical, they are not patentably distinct from each other for the following reasons. Claims 1-13 of U.S. Patent No. 6635462 are directed to a *Mycoplasma hominis* arginine deiminase comprising SEQ ID NO: 1 wherein said deiminase has been modified by elimination of at least one pegylation site at or adjacent to the catalytic region of the deiminase, as well as compositions comprising said modified deiminase. Claims 1-5 are directed to a *Mycoplasma hominis* arginine deiminase wherein said deiminase has been modified by elimination of at least one pegylation site at or adjacent to the catalytic region of the deiminase, as well as compositions comprising said modified deiminase. Therefore, claims 1-13 of U.S. Patent No. 6635462 anticipate claims 1-5 of the instant application as written.

Conclusion

23. No claim is in condition for allowance.

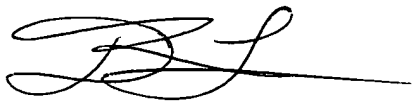
24. In June 2004, the USPTO ceased mailing paper copies of cited U.S. patents and U.S. patent application publications with all Office actions. See "USPTO to Provide Electronic Access to Cited U.S. Patent References with Office Actions and Cease Supplying Paper Copies," 1282 O.G. 109 (May 18, 2004). Foreign patent documents and non-patent literature will continue to be provided to the applicant on paper.

All U.S. patents and U.S. patent application publications are available free of charge from the USPTO web site (www.uspto.gov/patft/index.html), for a fee from the Office of Public Records (http://ebiz1.uspto.gov/oems25p/index.html), and from commercial sources. Copies are also available at the Patent and Trademark Depository Libraries (PTDLs). A list of the PTDLs may be found on the USPTO web site (www.uspto.gov/web/offices/ac/ido/ptdl/ptdlib_1.html). Additionally, a new feature in the Office's Private Patent Application Information Retrieval system (PAIR), E-Patent Reference, is available for downloading and printing of U.S. patents and U.S. patent application publications cited in U.S. Office Actions.

25. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PMR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

26. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Delia M. Ramirez whose telephone number is (571) 272-0938. The examiner can normally be reached on Monday-Friday from 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Ponnathapura Achutamurthy can be reached on (571) 272-0928. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.



Delia M. Ramirez, Ph.D.
Patent Examiner
Art Unit 1652

DR
March 16, 2006

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Qy     361 IGYDRNEKTNAALKAAGITVLPFHGNQLSLGMGNARCMSMPLSRKDVKW 409
           ||| |||||||||:|||| ||||||||||||||||||||||||||||||
Db     361 igysrnektnaaleaagikvlpfhgnqlslgmgnarcmsmplsrkdvkw 409


RESULT   5
AAW65454
ID   AAW65454 standard; Protein; 410 AA.
XX
AC   AAW65454;
XX
DT   19-NOV-1998  (first entry)
XX
DE   Arginine deiminase (ADI) amino acid sequence.
XX
KW   Arginine; ADI; recombinant; tumour; cancer; nitric oxide;
KW   nitric oxide synthase.
XX
OS   Mycoplasma arthritidis.
XX
PN   WO9833519-A1.
XX
PD   06-AUG-1998.
XX
PF   27-JAN-1998;   98WO-US01635.
XX
PR   31-JAN-1997;   97US-0792283.
XX
PA   (ENZO-) ENZON INC.
XX
PI   Filpula DR,  Wang M;
XX
DR   WPI; 1998-437174/37.
DR   N-PSDB; AAV07550.
XX
PT   Nucleic acid encoding arginine deiminase of Mycoplasma arthritidis -
PT   useful for, e.g. treating tumours, cancers and nitric oxide-related
PT   conditions
XX
PS   Claim 1; Page 33-34; 54pp; English.
XX
CC   This present sequence produces an arginine deiminase protein (ADI), an
CC   enzyme that hydrolyses arginine.  To obtain the ADI nucleic acid, the
CC   M. arthritidis strain 14152 was isolated from the american type culture
CC   collection, where from the arginine deiminase gene could be identified by
CC   the use of standard techniques.  The protein encoded by this gene can be
CC   produced recombinantly as well as naturally to treat ADI-susceptible
CC   conditions, particularly tumours and cancers, or nitric oxide-related
CC   conditions that require modulation of nitric oxide synthase.  It can also
CC   modulate the adverse effects of a low protein diet.
XX
SQ   Sequence   410 AA;

  Query Match             81.7%;  Score 1732.5;  DB 19;  Length 410;
  Best Local Similarity   80.5%;  Pred. No. 5.1e-157;
  Matches  330;  Conservative   38;  Mismatches   41;  Indels    1;  Gaps    1;

Qy       1 MSVFDSKFNGIHVYSEIGELETVLVHEPGREIDYITPARLDELLFSAILESHDARKEHQS 60
           |||||||| ||||||||||||||||||:||||||||||||||||||||||||||||:
Db       1 msvfdskfkgihvyseigeletvlvhepgkeidyitparldellfsaileshdarkehke 60

Qy      61 FVKIMKDRGINVVELTDLVAETYDLASKAAKEEFIETFLEETVPVLTEANKKAVRAFLLS 120
           ||  :| |||||||| ||: |||||||| |||: :| ||:::|||||:: ::  |: || |
Db      61 fvaelkkrginvvelvdlivetydlaskeakeklleefldds-vpvlsdehratvkkflqs 120

Qy     121 -KPTHEMVEFMMSGITKYELGVESENELIVDPMPNLYFTRDPFASVGNGVTIHFMRYIVR 179
            | |  :||:|::||||::| :||: |||||||||||||||||||||||||:||| ||
Db     121 qkstrslveymiagitkhdlkiesdlelivdpmpnlyftrdpfasvgngvtihymrykvr 180

Qy     180 RRETLFARFVFRNHPKLVKTPWYYDPAMKMPIEGGDVFIYNNETLVVGVSERTDLDTITL 239
           :|||||:|||| |||||| |||||||  : ||||||||||||:|||||||||| ||||
Db     181 qretlfsrfvfsnhpklvntpwyydpaegltieggdvfiynndtlvvgvsertdlqtitl 240
```

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Qy     240 LAKNIKANKEVEFKRIVAINVPKWTNLMHLDTWLTMLDKNKFLYSPIANDVFKFWDYDLV 299
           |||||||||| |||||||||||||||||||||||||||:||||||||||||||||||||
Db     241 laknikankecefkrivainvpkwtnlmhldtwltmldkdkflyspiandvfkfwdydlv 300

Qy     300 NGGAEPQPQLNGLPLDKLLASIINKEPVLIPIGGAGATEMEIARETNFDGTNYLAIKPGL 359
           |||  |||  |||||: || ||| |:| |||| ||||:::::| |||:||||||||: ||:
Db     301 nggdapqpvdnglpledllksiigkkptlipiagagasqidierethfdgtnylavapgi 360

Qy     360 VIGYDRNEKTNAALKAAGITVLPFHGNQLSLGMGNARCMSMPLSRKDVKW 409
           |||| |||||||||:|||||||| ||||||||||||||||||||||||||
Db     361 vigyarnektnaaleaagitvlpfrgnqlslgmgnarcmsmplsrkdvkw 410


RESULT   6
AAR05713
ID   AAR05713 standard; protein; 405 AA.
XX
AC   AAR05713;
XX
DT   16-AUG-1990  (first entry)
XX
DE   Arginine deaminase.
XX
KW   Arginine deaminase; carcinostatic; cancer; ds.
XX
PN   JP02053490-A.
XX
PD   22-FEB-1990.
XX
PF   16-AUG-1988;   88JP-0202759.
XX
PR   16-AUG-1988;   88JP-0202759.
XX
PA   (AGEN ) AGENCY OF IND SCI TECH.
XX
DR   WPI; 1990-103119/14.
DR   N-PSDB; AAQ03739.
XX
PT   Arginine deaminase gene -
PT   where DNA contains base sequence that codes amino acid sequence
PT   of arginine deaminase composing polypeptide.
XX
PS   Disclosure; Fig 1; 18pp; Japanese.
XX
CC   Expression vector transformed by the gene may be used to produce large
CC   quantities of arginine deaminase, useful as a carcinostatic.
XX
SQ   Sequence   405 AA;

  Query Match             77.0%;  Score 1632.5;  DB 11;  Length 405;
  Best Local Similarity   78.0%;  Pred. No. 1.8e-147;
  Matches  319;  Conservative   44;  Mismatches   41;  Indels    5;  Gaps    5;

Qy       2 SVFDSKFNGIHVYSEIGELETVLVHEPGREIDYITPARLDELLFSAILESHDARKEHQSF 61
           ||| |||||||||||:||:|||||||:|||||||||||||||||||| ||||||: |
Db       1 svfsdkfngihvyseigdlesvlvhepgkeidyitparldellfsailestdarkehkef 60

Qy      62 VKIMKDRGINVVELTDLVAETYDLASKAAKEEFIETFLEETVPVLTEANKKAVRAFLLS- 120
           |:|:| :|||||| ||| |||:|  |  :|: :: ||::: |||:   :|||  || |
Db      61 veilkkqginvvelvdlvvetynlvdkktqekllkdfldds-epvlspeqrkavekflksl 120

Qy     121 KPTHEMVEFMMSGITKYELGVESENELIVDPMPNLYFTRDPFASVGNGVTIHFMRYIVRR 180
           | | |::::|| |||||:||:::: |||||||| ||||||||||||||||:||| ||:
Db     121 kstkeliqymmggitkydlgikadkelivdpmpklyftrdpfasvgngvtihymrykvrq 180

Qy     181 RETLFARFVFRNHPKLVKTPWYYDPAMKMPIEGGDVFIYNNETLVVGVSERTDLDTITLL 240
           |||||::|:| |||||||| |||||||: |||||||||||:|||||||||||||||||||
Db     181 retlfskfiftnhpklvktp-yydpamklsieggdvfiynndtlvvgvsertdletitll 239

Qy     241 AKNIKANKEVEFKRIVAINVPKWTNLMHLDTWLTMLDKNKFLYSPIANDVFKFWDYDLVN 300
           ||||||||| |||||||||||| |||||||| ||||||:|||||||||||||| ||||||
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